Review article

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# Invasive techniques for prenatal diagnosis and therapy

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## 1 Introduction

The need for prenatal diagnosis of fetal disease in order to proceede to abortion or altered delivery management has stimulated the development of a range of techniques of fetal tissue biopsy. More recently, in utero therapy of some abnormalities has been possible such as direct blood transfusion for anemia or drainage of obstructed systems. Rapid improvements in ultrasound technology have not only increased the safety and success of amniocentesis, fetoscopy and placental biopsy but has also allowed the development of direct ultrasound guided techniques for fetal blood and tissue sampling.

Invasive procedures should only be performed when the benefits of the knowledge obtained outweigh the risks to the pregnancy. Such a decision can only be made in consultation with the parents and is affected by the prevailing moral views, as well as the safety, effectiveness and availability of the individual technique. Invasive procedures should only be performed after a thorough ultrasound examination to detect multiple pregnancy, fetal malformation and placental localization and confirm fetal viability and gestational age. Rhesus negative mothers should be given anti-D Ig G.

Accurate assessments of complications are difficult since only high risk pregnancies are offered invasive investigation. Spontaneous pregnancy problems are more common in this group and are likely to be attributed to the invasive test. Finding suitable control pregnancies is difficult while randomizing such patients is almost impossible.

In this article invasive methods of prenatal diagnosis and fetal therapy are discussed.

### Curriculum vitae

PETER SOOTHILL, *born in Worcestershire in 1957, graduated in medicine at Guy's Hospital in 1982. He has worked at King's College Hospital since 1983 training in Obstetrics and Gynaecology and in 1985 became a research fellow in the Harris Birthright Research Centre, learning the techniques of perinatal medicine, especially ultrasound scanning, chorion biopsy, and fetal blood sampling. His main research interest is fetal blood gases and acid-base balance.*

## 2 Techniques

### 2.1 Fetoscopy

Percutaneous, transabdominal, uterine endoscopy allows both the diagnosis of serious structural abnormalities, too small to be detected

ultrasonographically, and the visual guidance of fetal tissue biopsy [20]. Fetoscopy is done after 15 weeks' gestation; before this time the size of the uterus and amniotic fluid volume are too small for safe transabdominal entry. The most appropriate gestation depends on the procedure planned; for fetal examination orientation is easier with the smaller fetuses and clear amniotic fluid of 15–18 weeks, whereas fetal blood sampling is usually performed from 18 weeks onwards. After 20 weeks the amniotic fluid is cloudy but fetoscopy is possible until late in the third trimester.

By detailed ultrasound examination a site of entry can be identified which avoids damage to the placenta, umbilical cord or fetus but allows access to the fetal part being examined or biopsied. It is usually possible to find an area free of placenta even when the latter is anterior. Under sedation (which reduces fetal and maternal movements) and local anesthesia, a trocar and cannula (R. M. Surgical Developments, Croydon) is inserted transabdominally into the amniotic cavity using a full aseptic technique. A rigid fetoscope with fibre-optic illumination, such as the Olympus Selfoscope, then replaces the trocar (figure 1). It has a field of view of 55° and magnification, depending on distance from the object of up to 30 times. If required, a blood sampling needle or biopsy forceps can be passed through the side channel of the cannula.

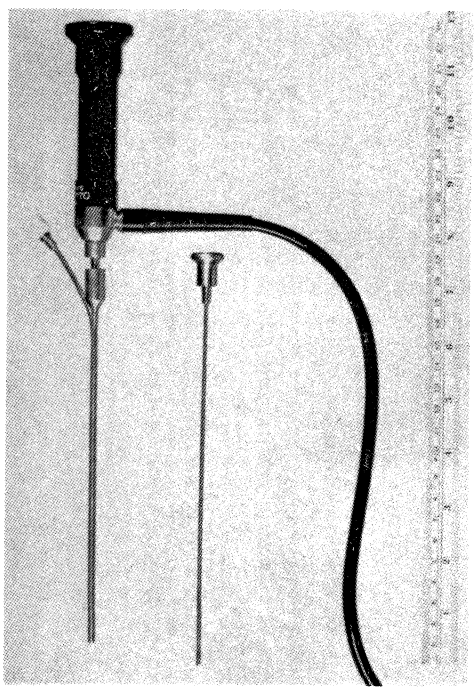

**Figure 1.** Olympus Selfoscope, trocar and cannula (R. M. Surgical Developments).

No major maternal complications have been reported in over 6000 fetoscopies (8th International Fetoscopy Meeting, 1985). The **risks** to the fetus depend on operator experience; in centers which have performed more than 100 fetoscopies the fetal mortality is less than 5% and in the largest series it is about 2%. Morbidity includes preterm labor (8–10%), amniotic fluid leakage (10%) and amnionitis (0.5%).

## 2.2 Ultrasound-guided procedures

Ultrasound allows the inspection of internal anatomy. By scanning in each of the three dimensions the site of entry, direction and depth required to reach an intended location can be selected. When a needle is inserted its tip can be identified by placing a real time curvi-linear ultrasound-transducer parallel to it, allowing the needle to be followed or guided (figures 2, 3). Some operators prefer sector or linear-array scanners and we use either depending on the uterine size.

There is less experience of ultrasound guided biopsy than fetoscopy and its **risks** need further evaluation but reports of ultrasound guided cord blood sampling are very encouraging.

**Invasive procedures to aid fetal imaging** are being developed. The instillation of ultrasound contrast media, such as physiological saline solution, into the amniotic cavity in severe oligohydramnios or into the fetal peritoneal cavity for better definition of a renal abnormality may be useful (unpublished observations).

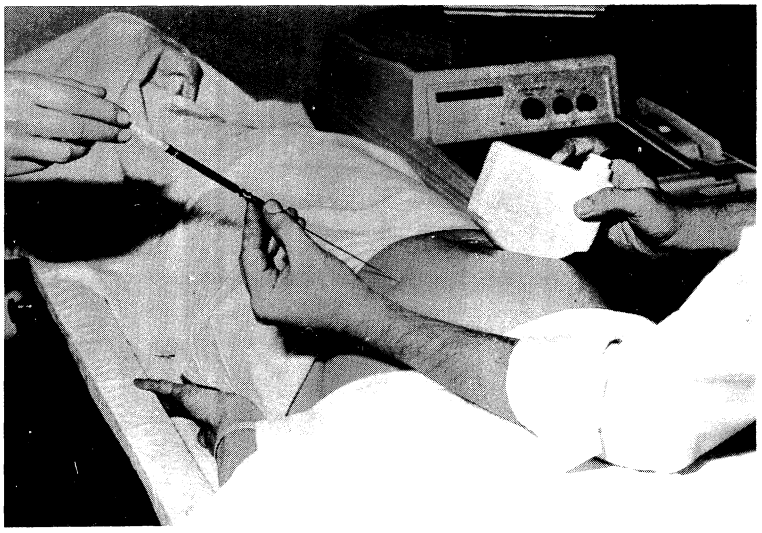

**Figure 2.** Ultrasound guided umbilical cord puncture for fetal blood sampling.

**Figure 3.** Ultrasound picture illustrating fetal blood sampling from the umbilical cord at the placental insertion, either fetoscopically or by ultrasound guided needling.

## 3 Prenatal diagnosis by fetal tissue biopsy

These techniques are restricted to patients at high risk as indicated by family history, advanced maternal age, abnormal maternal serum alpha-fetoprotein (MSAFP) or a structural abnormality detected by ultrasound scanning. A new indication may be suspected intrauterine hypoxia when estimation of fetal blood gas and acid-base status [16, 27, 28] may help to time the delivery.

The tissue that can give an accurate diagnosis as quickly as possible is the one selected for biopsy. This depends on the condition being investigated and each tissue is now considered in turn.

### 3.1 Amniotic fluid

Amniocentesis to diagnose inherited abnormalities is done at about 16 weeks gestation because the volume of amniotic fluid (150–200 ml) and concentration of viable cells is sufficient and the uterus is readily accessible transabdominally. The site of entry, direction and depth required to enter a pocket of fluid while avoiding fetal structures is identified. After antiseptic skin cleaning, a needle, usually 21 gauge, with or without a stillette, is inserted using a no-touch technique. Once through the skin it can be followed using real time ultrasound scanning to allow correction of the needle direction, if necessary, and to avoid a mobile fetus. The first 1 ml is discarded to avoid contamination with maternal blood and then 15–20 ml is aspirated.

Although amniocentesis is widely available its disadvantage is that it is done after 15 weeks and cytogenetic or enzymatic analysis requires cell culture which in practice takes 3–4 weeks resulting in much anxiety and a late termination of pregnancy in the event of an abnormality.

Amniocentesis can also be performed later in pregnancy to assess fetal lung maturity or the severity of rhesus disease and to diagnose amniotic infection. In the past it was used for amniography.

Three major collaborative studies on the **risks** of amniocentesis have been published. Two with a total of 2060 patients did not detect any increased risk after amniocentesis compared with matched controls or population data [13, 25]. One (2428 patients) found 1.7% more spontaneous abortions or stillbirths in the amniocentesis group [12]. However, the control group in the latter study had fewer pregnancy complications than expected.

### 3.2 Placental (chorionic villus) biopsy

Ultrasound guided placental biopsy can be done as early as 8 weeks gestation. Placenta has fetal genetic material and cytogenetic or DNA analysis potentially allows the diagnosis of any fetal genetic disease at an early stage of pregnancy. The rapid rate of cell division of this tissue means cytogenetic preparations can be made either directly [24] of following a short period of culture which allows a faster and earlier diagnosis than any other method. As the membranes are not punctured this may be the safest and quickest method of karyotyping at any gestation [17]. Although both blind and endoscopically guided placental biopsy have been tried, greater success in obtaining tissue with fewer complications has been found with ultrasound guided biopsy, either transcervically [30] or transabdominally [26].

A variety of instruments have been described for transcervical biopsy including polyethelene (Portex) or silver cannulae, biopsy forceps or endoscopes but the principle of passing the instrument through the cervix and into the placenta with ultrasound guidance is the same. The tissue obtained is examined microscopically and chorionic villi are identified and separated from decidual or blood contamination. For transabdominal placental biopsy a sector or curvi-linear scanner is used to direct a guide-needle through the abdominal wall and uterus into the placenta [26]. A finer biopsy needle is then inserted through the guide needle and villi are aspirated with a syringe. Repeated insertions of the fine needle are possible if the sample is inadequate. This technique is particularly suitable for later gestational ages when the cervix is a long way from the placenta and it may also have a lower risk of introducing infection than transcervical biopsy. However experience with this method is limited and it requires further investigation.

The main short-term **risk** of this procedure is that of miscarriage which occurs in 2–5% of pregnancies. The "expected" miscarriage rate for a control population has not yet been accurately established. Whether there is an increase in longer term sequelae e. g. IUGR, abruptio placentae or malformation is not known either. Small fetoplacental haemorrhages have been detected by MSAFP assay in about 50% of patients [31].

### 3.3 Blood

Fetal blood is valuable for the diagnosis of a large number of disorders and can be used to clarify equivocal results from other tissues, for example when detailed banding is required or after failure of, or mosaicism in, amniotic fluid cell culture [21]. Vessels in the chorionic plate (placentesis) or umbilical cord, or the fetal heart can be punctured. The needle can be guided either by fetoscopy [18] or by ultrasound [5].

Placentesis involves multiple punctures of the chorionic plate to produce bleeding into the amniotic fluid which is then aspirated and checked for the presence of fetal cells. This procedure has the risk of producing excessive fetal bleeding and there is a 10% fetal mortality.

Furthermore, contamination with amniotic fluid or maternal blood may make diagnosis difficult.

By fetoscopy the umbilical cord placental insertion can be identified and the vessels seen through the Whartons' jelly. This site has the advantages that blood coming from a cord vessel must be fetal and that hemostasis is excellent. Pure fetal blood can be achieved in 100% of patients but a particle size analyzer (Coulter Channelyzer) should be available to provide confirmation.

For ultrasound-guided needling of the cord, the placental insertion is identified sonographically. An entry site is chosen so that the needle approaches the cord nearly parallel to the intended vessel. If the placenta is anterior, a transplacental route is easiest and does not puncture the membranes. With a posterior placenta, a transamniotic approach may be necessary and is usually more difficult. Initial results are very encouraging, with high success and low complication rates [6]. This technique is a quick, outpatient procedure and has been used for antepartum diagnosis of fetal asphyxia by measuring fetal blood gases in high risk pregnancy [16, 27, 28]. Furthermore by sampling placental lakes of maternal blood it has been possible to study placental transfer [29].

The fetal heart has also been used as a source of blood [1]. A 1.2 mm guide needle is directed into the fetal thorax and a 0.6 mm diameter needle is passed down this into the left ventricle. The technique does not appear to have harmful effects on the fetal heart but it also needs further evaluation.

### 3.4 Skin

Fetal skin is required for the prenatal diagnosis of severe skin diseases that do not effect other systems and cannot yet be identified at the gene level. The fetoscope allows precise identification of the area to be biopsied and selection of the type of skin desired (e. g. a hairy area, such as the scalp or eyebrows, for the diagnosis of oculocutaneous albinism). The specimen is immediately examined microscopically by an experienced histologist to ensure adequacy of the biopsy.

Biopsy forceps can be passed down the fetoscope cannula after removal of the endoscope and the biopsy guided by ultrasound. Special skin biopsy instruments have also been devised which are inserted transabdominally and guided by ultrasound to the fetal skin. The great advantage of ultrasound in being able to "see" through tissues is not useful in this procedure whereas the ability to see surfaces in great detail makes fetoscopy espescially successful.

### 3.5 Liver

Some rare enzyme deficiencies of the urea cycle are expressed only in the liver eg. carbamyl phosphate synthetase and ornithine carbamyl transferase (OCT). They can be diagnosed prenatally using fetal liver [23], although a gene probe is available for some cases of OCT deficiency. By fetoscopy the right nipple and umbilicus are identified and a point half-way between these is chosen. A needle is inserted subcostally into the liver, strong suction is applied and the needle withdrawn, obtaining a core of tissue.

Similarly an ultrasound guided method has been described [9]. Ultrasound scanning allows identification of the needle tip within the liver.

### 3.6 Urine

When an obstruction of the fetal urinary system is detected by ultrasound examination, further investigation should include an assessment of residual renal function. A needle can be guided by ultrasound into the fetal bladder and urine aspirated for biochemical analysis. Furthermore after emptying the bladder the rate of refilling can be observed by serial ultrasound examinations. This information helps decide whether a vesico-amniotic shunt would be beneficial.

### 3.7 Tumors

Similar techniques to those for liver biopsy can be used for fetal tumors. We have diagnosed type 3 cystic adenomatoid malformation of the lung by ultrasound guided fetal lung biopsy at 20 weeks' gestation.

## 4 Fetal therapy

When the diagnosis of a potentially reversible or treatable fetal abnormality is made, the delivery should be in a specialist center. To prevent further damage or fetal death in utero due to a progressive lesion early delivery for surgery or therapy may be indicated. If the fetus is too premature for delivery in utero treatment may be considered. This should only be undertaken after exclusion of associated structural or chromosomal abnormalities and after demonstration that the primary lesion or its secondary effects are indeed progressive and that residual function compatible with postnatal life remains. Parents should be fully involved and warned of range of possible outcomes.

### 4.1 Blood transfusion

Severe rhesus isoimmunization can cause fetal anemia, hydrops fetalis and intrauterine death before the fetus is capable of extrauterine survival. Ultrasound scanning to time, guide and follow-up fetal transfusion and for monitoring during and between transfusions has greatly improved the prognosis of severely affected fetuses and has replaced the original X-ray techniques. Blood can be given into the fetal peritoneal cavity (IPT) [10] or intravascularly (IVT) [19]. A pure fetal blood sample is obtained using the methods described earlier and the fetal hemoglobin concentration and blood group determined and a direct Coomb's test performed. An empirical but safe estimate of the volume of blood to be given intraperitoneally is [7];

(gestation in weeks − 20) × 10 ml

Recently the volume of blood required for IVT has been calculated from previously obtained data on the feto-placental blood volume [14] and the donor and fetal hematocrits.

#### 4.1.1 Intraperitoneal transfusion

Under sedation and local anesthesia a 16-gauge Tuohy needle is inserted into the uterus so as to allow access to the antero-lateral aspect of the fetal abdomen. A linear-array, real-time ultrasound transducer is aligned so as to identify the needle-tip and fetal abdomen. The needle is inserted into the peritoneal cavity between the umbilicus and bladder and any ascites aspirated. The needle position is confirmed by a 4−5 ml injection of isotonic saline and then packed adult blood, compatible with the mothers', is injected through the needle at a rate of 3−5 ml/min. IPT can also be performed with combined fetoscopic and sonographic guidance by passing a 21 gauge Tuohy needle (R. M. Surgical Developments) down the side arm of the fetoscope cannula. This may be done, after a fetal blood sample has been taken, when the amniotic fluid is very cloudy, in early pregnancy (eg. < 20 weeks), or when a large volume of blood is required, in combination with IVT.

#### 4.1.2 Intravascular transfusion

After fetal blood sampling with fetoscopic or ultrasonic guidance (for hematocrit estimation with a Coulter Channelyzer) the needle tip is kept in the lumen of the vessel and donor blood is injected at a rate of 1−3 ml/min, while observing the fetal heart continuously with ultrasound. The aim is to achieve a final fetal hematocrit of 35−45% and this is checked by aspirating a post-transfusion sample. There is much greater experience of this technique by fetoscopy [22]. Exchange transfusion has been performed fetoscopically before mid-trimester abortion [11] but the risk to continuing pregnancies seems to be greater than "top-up" transfusion.

Alternative methods of IVT include ultrasound-guided puncture of the intrahepatic umbilical vein [2] or fetal heart. Experience with

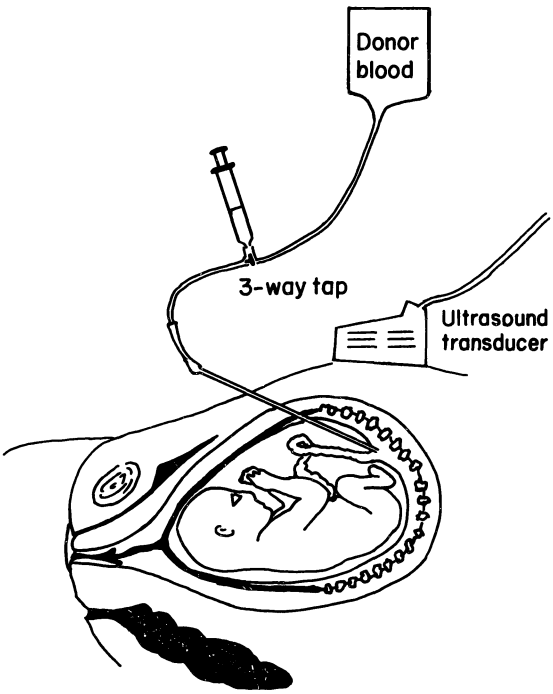


**Figure 4.** Ultrasound guided intravenous fetal blood transfusion in rhesus disease.

these methods however, is too small for accurate assessment of efficiency and risks. We have recently used an ultrasound-guided cord puncture technique and infused blood through the same needle after determination of the fetal hematocrit (figure 4).

### 4.1.3 Albumin infusion

Fetuses with non-immune hydrops have very low blood albumin concentrations [15] and it has been suggested that the low oncotic pressure increases the loss of fluid from the vascular compartment. We have given albumin infusions to several fetuses but the results need further evaluation.

## 4.2 Drainage procedures

Obstruction of fetal systems can cause dilatation and damage to both the primary organ and the adjacent structures. By-passing the obstruction and reducing the pressure may prevent further damage until delivery when more definitive surgery is possible. These procedures are only helpful if there is no major untreatable abnormality and if useful residual organ function remains.

### 4.2.1 Obstructive uropathy

Complete obstruction of the urinary system from an early gestation leads to renal dysplasia and absence of renal function. Incomplete or late onset obstruction may allow good renal development but still compromise renal function to a degree that depends on the duration and completeness of obstruction. Renal parenchymal thickness and consistency, assessed ultrasonographycally, and urine biochemistry can help to estimate residual renal function [21].

Experimental work suggested that relief of obstruction in utero was beneficial [8] and subsequently suprapubic insertion of a vesico-amniotic shunt was performed in several centers. A cannula (Rocket of London) is guided into the distended fetal bladder by ultrasound. Through this, a double "pig-tail" catheter is introduced so that one end curls up inside the bladder and the other outside the fetal trunk in the amniotic cavity. Urine is thus released, amniotic fluid is formed, and the secondary complications of both renal damage and oligohydramnios can be reduced in some cases.

### 4.2.2 Obstructive hydrocephalus

High-pressure ventricular dilatation causes brain damage. After delivery, ventricular shunting limits further structural damage and may improve the prognosis. If prematurity prevents delivery and there is sonographic evidence of increasing ventriculomegaly, in utero drainage could be beneficial.

Repeated ultrasound guided cerebro-spinal fluid (CSF) aspiration (encephalocetesis) has been attempted but ventricular dilatation still

occured because of rapid reaccumulation [3]. Ventriculo-amniotic shunts, with a one-way valve allowing CSF out of the brain, have been inserted under ultrasound guidance [4]. Reduction in ventricular dilatation has been achieved but follow-up developmental studies have been discouraging (Fetal Surgery Registry 1986) and major problems have been experienced in maintaining shunt patency and position.

### 4.2.3 Pleural effusions

Fetal pleural effusions can occur as part of generalised hydrops fetalis or as an isolated abnormality (chylothorax) and prevent expansion and development of the fetal lung. A pleuro-amniotic shunt can be inserted with ultrasound guidance using similar equipment to that described for bladder catheterization. We have now treated four such fetuses in this manner and in one, associated generalized hydrops was reversed. Post-natal outcome in these babies has been excellent.

### 4.2.4 Cyst aspiration

Large fetal cysts occur as an isolated abnormality or as part of a syndrome (e. g. cystic hygromata in Turner's syndrome). Pressure effects or obstruction at delivery may be prevented by needle puncture and aspiration.

## 4.3 Drug therapy

Fetal drug therapy such as digoxin in hydrops fetalis or anti-arrhythmic agents for fetal cardiac arrhythmias is usually administered across the placenta through the mother [32]. Substances that are not adequately transferred may be injected into the amniotic cavity or directly into the fetal blood stream. For resuscitation of previable fetuses with reversible causes of cardiovascular collapse transplacental therapy is too slow. We have successfully administered adrenaline, calcium and atropine directly to fetuses when cardiac arrest occured during an invasive procedure such as blood transfusion (unpublished).

**Keywords:** Fetal therapy, fetal tissue biopsy, fetoscopy, prenatal diagnosis, ultrasound guided needle biopsy.

**Zusammenfassung**

**Invasive Techniken zur pränatalen Diagnose und Therapie** Bei der **Fetoskopie** wird ein Endoskop transabdominal in die Amnionhöhle vorgeschoben und somit die Diagnose kleiner struktureller Defekte sowie die Biopsie von fetalem Gewebe unter Sichtkontrolle ermöglicht. Mit Hilfe des Ultraschalls wird der Zugang so gewählt, daß sich das Endoskop an dem fetalen Abschnitt, der untersucht oder biopsiert werden soll, befindet und eine Verletzung der Plazenta, der Nabelschnur oder des Feten vermieden wird.

Die **Nadelbiopsie unter Ultraschallkontrolle** wird heute zur Gewinnung verschiedener fetaler Gewebe eingesetzt. Die Nadel kann durch die gleichzeitige Untersuchung mit einem Real-time-Ultraschalltransducer in den Geweben identifiziert und somit richtig geführt werden.

**Pränatale Diagnose durch fetale Gewebeentnahme:** Zur Diagnose vererbter Erkrankungen wird um die 16. Schwangerschaftswoche, nämlich dann, wenn die Fruchtwassermenge und die Konzentration fetaler Zellen ausreichend sind und der Zugang zum Uterus möglich ist, eine **Amniozentese** durchgeführt. Zunächst werden die optimale Punktionsstelle, Richtung und Tiefe zum Erreichen eines Fruchtwasserpools bestimmt und dann eine 20 gauge-Nadel unter Ultraschallkontrolle eingeführt. Der Nachteil dieser Methode ist, daß sie erst nach der 15. Woche durchgeführt werden kann und für die Diagnose Zellkulturen angelegt werden müssen, so daß die Frauen sehr lange besorgt sind und im Falle eines pathologischen Befundes die Schwangerschaftsbeendigung sehr spät erfolgt.

Die **Chorionzottenbiopsie** unter Ultraschallkontrolle wird normalerweise frühestens in der 8. Schwangerschaftswoche durchgeführt. Bei der transzervikalen Biopsie wurden verschiedene Kanülen, Biopsiezangen und Endoskope eingesetzt. Prinzipiell gibt es jedoch beim Einbringen des Instrumentes durch die Zervix in die Plazenta unter Ultraschallkontrolle keine Unterschiede. Bei der transabdominalen Biopsie wird die Nadel durch die Bauchwand und den Uterus in die Plazenta eingeführt. Diese Methode eignet sich speziell für spätere Schwangerschaftswochen und ist möglicherweise mit einem geringeren Infektionsrisiko behaftet als die trans-

zervikale Biopsie. Wir konnten kürzlich zeigen, daß zu jedem Schwangerschaftsalter ein fetaler Karyotyp aus Plazentagewebe erstellt werden kann.

Fetales **Blut** kann durch Punktion der Nabelschnur an der plazentaren Insertionsstelle gewonnen werden. Der Nabelschnuransatz kann fetoskopisch oder sonographisch identifiziert werden, und die Nadel wird in eines der Gefäße eingeführt. Für die pränatale Diagnose einiger schwerer Hauterkrankungen wird fetales **Hautmaterial** benötigt. Die Biopsiezange kann durch einen zweiten Zugang am Fetoskop eingeführt werden. Einige seltene Enzymdefekte des Harnstoffzyklus sind nur in **Leberzellen** nachweisbar. Infrakostal wird eine Nadel in die Leber eingeführt und nach Absaugen Lebergewebe gewonnen. Mit der gleichen Technik können **fetale Tumoren** biopsiert und histologisch untersucht werden. Bei Feten mit obstruktiven Harnwegserkrankungen kann eine **Urinprobe** entnommen werden, um über die biochemische Analyse die Nierenfunktion zu erfassen. Nach Entleeren der Blase kann per Ultraschall die Auffüllung beobachtet werden. Dies stellt eine Entscheidungshilfe dar, ob ein vesiko-amnialer Shunt günstig ist oder nicht.

**Fetale Therapie:** Zur **intraperitonealen Transfusion** (IPT) wird eine 16 gauge-Tuohynadel unter Ultraschallkontrolle zunächst in den Uterus und dann in das fetale Abdomen zwischen Nabel und Harnblase eingeführt. Mit dem mütterlichen Blut kompatible Erythrozytenkonzentrate von Erwachsenen werden mit einer Geschwindigkeit von 3–5 ml/min infundiert. Die **intravaskuläre Transfusion** (IVT) wird so durchgeführt, daß nach einer Blutabnahme unter fetoskopischer oder sonographischer Kontrolle die Nadelspitze im Gefäßlumen bleibt und dann Spenderblut infundiert wird. Angestrebt wird ein fetaler Hämatokrit von 35–45%. Bei Feten mit nicht-immunologischem Hydrops haben wir bei sehr niedrigen Albuminwerten im Plasma Albumin infundiert.

**Drainagen:** Für einige Feten mit **obstruktiven Harnwegserkrankungen** ist eine Drainage in utero günstig. In der überdehnten Blase wird unter Ultraschallkontrolle eine Kanüle plaziert und dadurch ein doppelter „pig-tail"-Katheter eingeführt, so daß sich ein Ende innerhalb der Blase aufwickelt und das andere in der Amnionhöhle. Der Urin kann abfließen, Fruchtwasser gebildet werden und die sekundären Komplikationen sowohl einer renalen Schädigung wie auch eines Oligohydramnions können in einigen Fällen reduziert werden. Bei Neugeborenen mit **Hydrozephalus** kann ein Ventrikelshunt die Hirnschädigung reduzieren. Wenn wegen Prämaturität eine Entbindung nicht möglich ist, kann ein ventrikulo-amnialer Shunt mit einer one-way-Klappe, durch die der Liquor abfließen kann, unter Ultraschallkontrolle eingesetzt werden. Man kann so die Ventrikeldilatation vermindern; die Ergebnisse von Nachuntersuchungen zur Erfassung der körperlichen und geistigen Entwicklung waren jedoch entmutigend. **Pleuraergüsse** behindern die Ausdehnung und Entwicklung der fetalen Lunge. Pleuro-amniale Shunts, die nach dem gleichen Prinzip wie die oben beschriebene Blasenkatheterisierung funktionieren, können hier eingesetzt werden. Große fetale **Zysten** können abgesaugt werden, um Druckschäden oder auch Geburtshindernisse zu vermeiden.

**Medikamentöse Therapie:** Wenn Medikamente nicht oder zu langsam die Plazenta passieren, kann die direkte Applikation an den Feten versucht werden. Wenn während eines invasiven Eingriffes ein kardiovaskulärer Kollaps auftrat, konnten wir stark deprimierte Feten durch intravenöse oder intramuskuläre Gaben von Adrenalin, Kalzium und Atropin erfolgreich reanimieren.

**Schlüsselwörter:** Fetale Gewebeentnahme, fetale Therapie, Fetoskopie, Nadelbiopsie unter Ultraschallkontrolle, pränatale Diagnose.

**Résumé**

**Techniques invasives pour le diagnostic et la thérapeutique prénatales**

La **feotoscopie** nécessite l'insertion transabdominale d'un endoscope dans la cavité amniotique. Elle permet à la fois le diagnostic d'anomalies structurales minimes et la réalisation de biopsies tissulaires fœtales sous le contrôle de la vue. On localise par échographie le site d'abord permettant l'accès aux régions fœtales à examiner ou à biopsier, tout en évitant les lésions du placenta, du cordon ombilical ou du fœtus.

On a récemment étendu à de nombreux tissus fœtaux les **biopsies à l'aiguille sous contrôle échographique.** On peut visualiser une aiguille à l'intérieur des tissus en plaçant une sonde d'échographie en temps réel parallèlement à elle, ce qui permet de guider l'aiguille.

**Diagnostic prénatal par biopsie de tissus fœtaux: L'amniocentèse** à visée diagnostique des anomalies héréditaires est effectuée à environ 16 semaines de gestation lorsque le volume de liquide amniotique, la concentration cellulaire et l'accessibilité à l'utérus sont adéquats. Sous contrôle échographique en temps réel on repère le point de ponction, la direction et la profondeur nécessaires pour atteindre une poche de liquide amniotique et on intraduit une aiguille de calibre 20. L'inconvénient de cette technique est qu'elle est effectuée après 15 semaines et que l'analyse nécessite en règle générale une culture cellulaire ce qui entraîne une anxiété prolongée et une interruption tardive en cas d'anomalies.

La **biopsie placentaire** (villosités chorioniques) écho-guidée est habituellement réalisée dans la 8ème semaine de gestation. On a utilisé bon nombre de canules, de pinces à biopsie et d'endoscopes pour ces biopsies placentaires par voie transcervicale, mais le principe du passage des instruments à travers le col et à l'intérieur du placenta

sous contrôle échographique est le même. Pour la biopsie placentaire transabdominale on introduit une aiguille à travers la poroi abdominale et l'utérus dans le placenta. Cette méthode est particulièrement adaptée pour les âges gestationnels plus tardifs et elle présente un risque moindre d'introduire une infection que par la voie transcervicale. Nous avons récemment montré que l'on peut réaliser le caryotype sur les tissus placentaires pour toute grossesse.

Le **sang fœtal** est obtenu par ponction du cordon ombilical au niveau de son insertion placentaire. On peut localiser l'insertion du cordon par fœtoscopie ou par échographie, et on introduit l'aiguille dans un des vaisseaux. Pour le diagnostic prénatal de certaines affections cutanées graves il faut de la **peau fœtale.** On peut faire passer la pince à biopsie dans le canal latéral du fœtoscope. Certains déficits enzymatiques rares du cycle de l'urée ne s'expriment qu'au niveau **hépatique.** On introduit une aiguille en sous-costal dans le foie et par aspiration on obtient un fragment tissulaire.

**Therapeutique fœtale:** Pour les **transfusions intrapéritonéales** (IPT) on introduit dans l'utérus puis dans l'abdomen fœtal, entre l'ombilic et la vessie, une aiguille de Tuohy de calibre 16, sous contrôle échographique. On injecte du sang adulte, compatible avec la mère, au rythme d'environ 3 à 5 ml/min. Les **transfusions intra-vasculaires** sont réalisées après prélèvement de sang fœtal par fœtoscopie ou sous contrôle échographique, l'extrémité de l'aiguille laissée en place dans la lumière vasculaire, on injecte du sang de donneur. Le but est d'obtenir à la fin un hématocrite fœtal de 35–45%. Nous avons réalisé des perfusions d'albumine chez des fœtus présentant un hydrops non immunologique, lorsque les concentrations d'albumine plasmatique étaient très basses.

**Techniques de drainage:** Certains fœtus présentant une **uropathie obstructive** peuvent bénéficier d'un drainage in utero. On introduit dans la vessie distendue sous contrôle échographique une canule à travers laquelle on fait passer un catheter double «queue de cochon» de telle sorte que l'une des extrémités forme une boucle à l'intérieur de la vessie et l'autre en dehors du tronc fœtal dans la cavité amniotique. L'urine est libérée, le liquide amniotique se forme, et les complications secondaires et de la souffrance rénale et de l'oligoamnios peuvent être diminuées dans certains cas. Les shunts ventriculaires néonataux pour **hydrocéphalie** peuvent diminuer les lésions cérébrales, et lorsque la prématurité empêche l'accouchement on peut mettre en place sous contrôle échographique un shunt ventriculo-amniotique à l'aide d'une valve à une voie, ce qui permet l'issue du LCR en dehors du cerveau. On obtient ainsi une réduction de la dilatation ventriculaire, mais les études du suivi du développement ne sont pas encourageantes. Les **épanchements pleuraux** interfèrent avec l'expansion et le développement des poumons fœtaux. On peut installer des shunts pleuro-amniotiques en utilisant un matériel similaire à celui décrit pour le cathétérisme vésical. On peut aspirer les **kystes** fœtaux volumineux pour éviter une compression ou un obstacle lors de l'accouchement.

**Traitements médicamenteux:** On a essayé d'administrer des médicaments directement au fœtus quand ils ne traversent pas le placenta de façon adéquate ou quand le transfert est trop lent. Nous avons réanimé avec succès des fœtus avant la viabilité à l'aide d'adrénaline, de calcium et d'atropine en intraveineux ou en intra-musculaire lorsque survient un collapsus cardio-vasculaire au cours des techniques invasives.

**Mots-clés:** Biopsie à l'aiguille écho-guidée, biopsie de tissus fœtaux, diagnostic prénatal, fœtoscopie, thérapeutique fœtale.

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